ORIGINAL ARTICLE

Comparison of nutritional and immunological scoring systems predicting prognosis in T1-2N0 colorectal cancer

Guangzhe Pian[1,2,3] · Seung Yeop Oh[1]

Abstract

Purpose Previous studies have shown that the new nutritional and immunological status scoring systems of the Naples prognostic score (NPS), controlling nutritional status score (CONUT), and the older prognostic nutritional index (PNI) are independent predictors in colorectal cancer. This study compares the prognostic value of NPS, CONUT, and PNI in T1–2N0 colorectal cancer.

Methods We retrospectively evaluated 305 consecutive stage I (T1-2N0M0) colorectal cancer patients who underwent radical surgery from January 2010 to December 2015 at our hospital. The NPS results were divided into 3 groups (0, 1, and 2 groups), and the PNI and CONUT results were divided into 2 groups (low and high groups).

Results The patients with low PNI had worse overall survival (OS) and disease-free survival (DFS) than those with high PNI ($P < 0.001$ and $P < 0.001$, respectively). Multivariate analysis showed that PNI was independently associated with OS and DFS ($P < 0.001$ and $P < 0.001$, respectively), but NPS and CONUT results were not.

Conclusion The PNI is an independent predictor in stage I colorectal cancer, but NPS and CONUT results are not.

Keywords Colorectal cancer · T1-2N0M0 · Prognostic nutritional index · Controlling nutritional status score · Naples prognostic score

Introduction

Colorectal cancer (CRC) is the third most common cancer and one of the most common causes of cancer death worldwide [1]. Treatment strategies and prognoses for CRC are mainly based on the American Joint Committee on Cancer (AJCC) TNM pathological stages [2, 3]. Both stage I (T1-2N0M0) and stage II (T3-4N0M0) CRC, in which regional lymph node metastases are absent, have a good prognosis. For stage II disease, some risk factors have been published, and treatment strategies based on those risk factors could significantly improve survival. However, few risk factors have been published for stage I disease, even though

recurrence is possible. If treatment strategies could be based on risk factors for stage I disease, as they are for stage II disease, patient outcomes might improve.

Studies have shown that malnutrition and immunological status play a critical role in development of cancers [4, 5]. Therefore, several scores based on nutritional and immunological status have been established to predict the prognosis of CRC. The prognostic nutritional index (PNI) was established in 1980 and reported as an independent predictor for CRC outcomes [6, 7]. Iseki et al. [8] first reported in 2015 that the controlling nutritional status score (CONUT) was an independent outcome predictor for patients with CRC undergoing surgery. In addition, the Naples prognostic score (NPS) was established in 2017 and reported to be an independent outcome predictor for patients with CRC undergoing surgery [9]. Galizia et al. [9] argued that the prognostic value of the NPS was better than that of both CONUT and PNI. Most previous studies assessing the prognostic value of CONUT, NPS, and PNI used patients with disease stages I to IV [7, 9, 10]. However, we suggest that the prognostic values of those indexes should be assessed separately at each stage. Disease progression at different stages produces different

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nutritional and immunological statuses which may lead to different prognostic values or cut-off values. If the prognostic values and cut-off values of stage I CRC are clarified, it will help the clinicians to provide different treatment strategies or follow-up systems to improve the outcomes. The aim in this study was to evaluate and compare the prognostic value of PNI, CONUT, and NPS in stage I CRC.

Patients and methods

Patients

We studied the medical records of 367 patients who were diagnosed with stage I (T1-2N0M0) CRC and underwent a curative resection at Ajou University Hospital from January 2010 to December 2015. The inclusion criteria were as follows: (1) histologically confirmed adenocarcinoma, (2) stage I according to the 8th edition of the AJCC TNM, and (3) radical surgery. The exclusion criteria were as follows: (1) history of other cancers ($n = 39$), (2) chemotherapy or radiation therapy before surgery ($n = 12$), (3) death within 1 month after surgery ($n = 2$), and (4) non-adenocarcinoma or unknown histology ($n = 9$). Finally, 305 patients were enrolled in the study.

Data collection

The clinicopathological data analyzed were sex, age, body mass index (BMI), location, histology, tumor size, number of retrieved lymph nodes, lymphatic invasion, and perineural invasion.

Blood samples were analyzed for albumin, cholesterol, neutrophil count, lymphocyte count, and monocyte count less than 2 weeks before surgery. The PNI, neutrophil-to-lymphocyte ratio (NLR), and lymphocyte-to-monocyte ratio (LMR) were calculated using the following formulas: PNI $= 10 \times$ albumin (g/dl) $+ 0.005 \times$ total lymphocyte count (/mm^3); NLR $=$ neutrophil count/lymphocyte count; LMR $=$ lymphocyte count/monocyte count. CONUT was calculated using albumin, total lymphocyte count, and total cholesterol (Table 1). The NPS was calculated using albumin, total cholesterol, NLR, and LMR (Table 1).

Patients were seen every 3–6 months for the first 2 years after surgery, every 6 months for the next 3 years, and every year thereafter. Routine physical examinations and carcinoembryonic antigen (CEA) assays were performed at each follow-up visit. Abdominopelvic computed tomography scanning (CT), chest X-ray, and colonoscopy were performed every year and when recurrence was suspected.

Recurrence was determined by radiographic examination and/or histological confirmation through biopsy.

Table 1 Controlling nutritional status (CONUT) scoring system and Naples prognostic (NPS) scoring system

CONUT	Normal	Light	Moderate	Severe
Albumin (g/dl)	≥ 3.50	3.00–3.49	2.50–2.99	< 2.50
Score	0	2	4	6
Total lymphocyte count	≥ 1600	1200–1599	800–1199	< 800
Score	0	1	2	3
Total cholesterol (mg/dl)	≥ 180	140–179	100–139	< 100
Score	0	1	2	3
Total score	0–1	2–4	5–8	9–12
NPS	Group 0	Group 1	Group 2	
Albumin (g/dl)	≥ 4	< 4		
Score	0	1		
Total cholesterol (mg/dl)	> 180	≤ 180		
Score	0	1		
NLR	≤ 2.96	> 2.96		
Score	0	1		
LMR	> 4.44	≤ 4.44		
Score	0	1		
Total score	0	1–2	3-4	

NLR neutrophil-to-lymphocyte ratio; *LMR* lymphocyte-to-monocyte ratio

The cut-off date for follow-up was July 2020, and the median follow-up time was 87.0 months (range, 3–125 months). During this period, 21 patients (6.89%) died, and 16 patients (5.25%) experienced recurrence. Overall survival (OS) was defined as the period from surgery to death from any cause or to the last follow-up. Disease-free survival (DFS) was defined as the period from surgery to recurrence, death, or last follow-up.

This study had full ethical approval from the Institutional Review Board of Ajou University School of Medicine.

Statistical analysis

Using X-tile 3.6.1 software (Yale University, New Haven, CT, USA), we determined the cut-off value for a continuous PNI of 49.3, which we identified from the minimum *P*-value according to the OS (Supplementary Fig. S1) [11]. The total CONUT score cut-off value was set at 3, which is in line with most previous studies [8] [12, 13]. We then divided the patients into high (PNI > 49.3) and low (PNI ≤ 49.3) PNI groups and high (score ≥ 3) and low (score < 3) CONUT groups. Patients were divided by NPS score into group 0, group 1, and group 2, which is in line with the previous study [9]. A Pearson's x^2 or Fisher's exact test was performed to assess differences between PNI and clinicopathological characteristics. Survival curves were evaluated using the Kaplan–Meier method and were compared using log-rank test. Independent predictors were determined using

multivariate Cox regression analyses of OS and DFS. The variables with $P < 0.20$ in univariate analysis were included in multivariate analysis. $P < 0.05$ was considered statistically significant. Statistical analyses were performed using SPSS version 25.0 (IBM, Armonk, NY, USA) and GraphPad Prism 7 (GraphPad Software Inc., La Jolla, CA, USA).

Results

Clinicopathological characteristics

Table 2 shows that the median age was 63 (range: 25–87), and 183 males and 122 females were included in the cohort. The CONUT was normal (score 0–1) for 224 (73.44%) patients, light (score 2–4) for 80 (26.23%) patients, moderate (score 5–8) for 1 (0.33%) patient, and severe for none. By NPS score, group 0 (score 0) comprised 77 (25.25%), group 1 (score 1–2) was 199 (65.24%), and group 2 (score 3–4) was 29 (9.51%) patients. There were 38 (12.46%) patients with PNI ≤ 49.3 and 267 (87.54%) patients with PNI > 49.3.

Survival analysis according to the PNI, CONUT, and NPS

The low PNI group had significantly worse OS and DFS than the high PNI group ($P < 0.001$ and $P < 0.001$, respectively) (Fig. 1A and B). The high CONUT group also had significantly worse OS and DFS than did the low CONUT group ($P = 0.020$ and $P = 0.045$, respectively) (Fig. 2A and B). However, OS and DFS did not differ among the three NPS groups ($P = 0.201$ and $P = 0.478$, respectively) (Fig. 3 A and B).

Univariate and multivariate analyses for OS and DFS

The univariate analysis for OS showed that P value for age (hazard ratio [HR], 4.846; 95% confidence interval [CI], 1.630–14.405; $P = 0.005$), histology (HR, 3.020; 95% CI, 0.702–12.983; $P = 0.137$), location (HR, 1.848; 95% CI, 0.778–4.385; $P = 0.164$), perineural invasion (HR, 10.461; 95% CI, 1.380–79.304; $P = 0.023$), albumin (HR, 0.188; 95% CI, 0.025–1.406; $P = 0.104$), PNI (HR, 0.118; 95% CI, 0.050–0.278; $P < 0.001$), and CONUT (HR, 3.373; 95% CI, 1.135–10.026; $P = 0.029$) (Table 3). In multivariate analysis, only PNI (HR, 0.141; 95% CI, 0.054–0.371; $P < 0.001$) was significantly associated with OS (Model 2, Table 4).

Univariate analysis for DFS showed that P values for location (HR, 2.336; 95% CI, 0.849–6.427; $P = 0.100$), perineural invasion (HR, 18.461; 95% CI, 2.432–140.108; $P = 0.005$), CEA (HR, 2.659; 95% CI, 0.758–9.330; $P = 0.127$), albumin (HR, 0.141; 95% CI, 0.019–1.069; $P = 0.058$), PNI (HR, 0.097; 95% CI, 0.036–0.260; $P < 0.001$), and CONUT (HR,

Table 2 Clinicopathological features of patients

Variables	N (%)
Sex	
Male	183 (60.00)
Female	122 (40.00)
Median age (range, y)	63 (25–87)
BMI	
< 25 kg/m^2	209 (68.52)
≥ 25 kg/m^2	96 (31.48)
Location	
Colon	176 (57.70)
Rectum	129 (42.30)
Histology	
Well	104 (34.10)
Moderately	190 (62.30)
Poorly	11 (3.60)
Tumor size	
≤ 2 cm	156 (51.15)
> 2 cm	149 (48.85)
T stage	
T1	164 (53.77)
T2	141 (46.23)
Number of retrieved LNs	
< 12	95 (31.15)
≥ 12	210 (68.85)
Lymphatic invasion	
Negative	274 (89.84)
Positive	31 (10.16)
Perineural invasion	
Negative	303 (99.34)
Positive	2 (0.66)
CEA	
≤ 5.0 ng/mL	279 (91.48)
> 5.0 ng/mL	26 (8.52)
Albumin	
< 3.5 g/dl	3 (0.98)
≥ 3.5 g/dl	302 (99.02)
CONUT	
Normal (0–1)	224 (73.44)
Light (2–4)	80 (26.23)
Moderate (5–8)	1 (0.33)
Severe (9–12)	0
NPS	
Group 0 (0)	77 (25.25)
Group 1 (1–2)	199 (65.24)
Group 2 (3–4)	29 (9.51)
PNI	
≤ 49.3	38 (12.46)
> 49.3	267 (87.54)

BMI body mass index, *LN* lymph node, *CEA* carcinoembryonic antigen, *CONUT* controlling nutritional status score, *NPS* Naples prognostic score, *PNI* prognostic nutritional index
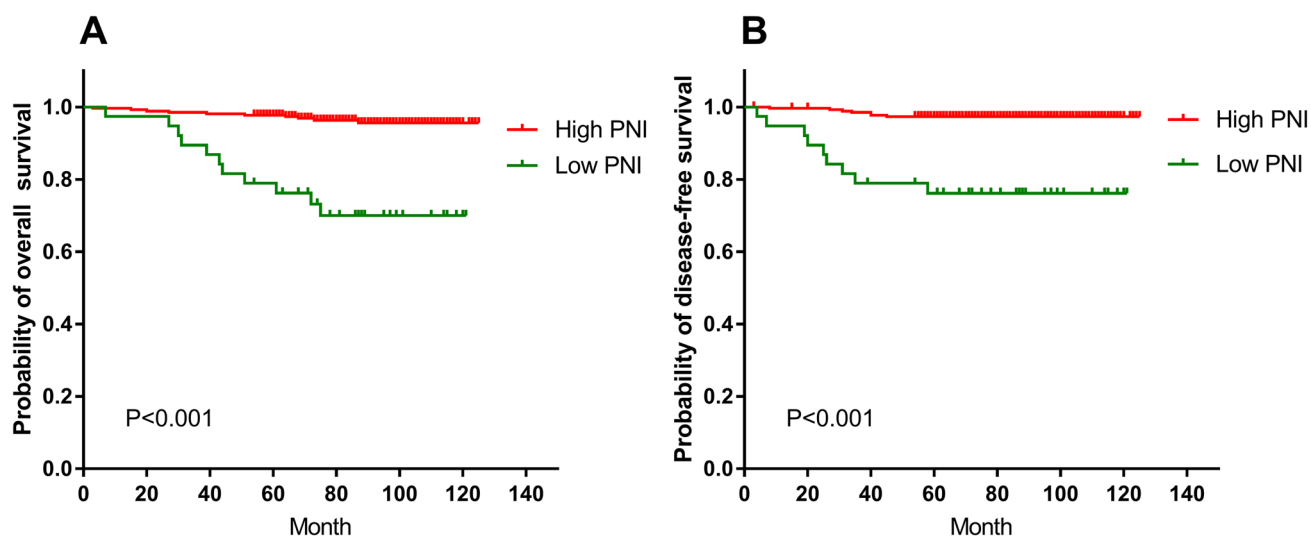
Fig. 1 Survival rates between high and low PNI groups. **A** Overall survival in the two groups. **B** Disease-free survival in the two groups

3.353; 95% CI, 0.955–11.766; $P = 0.059$) were less than 0.2 (Table 3). In multivariate analysis, both perineural invasion (HR, 20.084; 95% CI, 2.126–189.717; $P = 0.009$) and PNI (HR, 0.105; 95% CI, 0.037–0.297; $P < 0.001$) were significantly associated with DFS (Model 5, Table 4).

Re-determined the NPS and survival analysis

Using the X-tile software, re-determined the NPS: albumin (normal: ≥ 4.2 g/dL), total cholesterol (normal: > 189 mg/dL), NLR (normal: ≤ 2.3), and LMR (normal: > 4.9). Survival analysis revealed OS significant difference among the three new-NPS groups ($P = 0.002$), but DFS did not differ among the three new-NPS groups ($P = 0.559$) (Fig. 4 A and B). In the univariate analysis, the new-NPS was

significantly associated with OS ($P = 0.036$), but not in multivariate analysis ($P = 0.085$). About DFS, in the univariate analysis, the new-NPS was not significantly associated with DFS ($P = 0.586$).

Survival analysis of PNI in colon and rectal cancer

In colon cancer, the patients with low PNI had significantly worse OS and DFS compared to the patients with high PNI ($P < 0.001$ and $P < 0.001$, respectively) (Fig. 5 A and B). Similarly, in rectal cancer, the low PNI group had significantly worse OS and DFS ($P < 0.001$ and $P < 0.001$, respectively) (Fig. 6A and B).
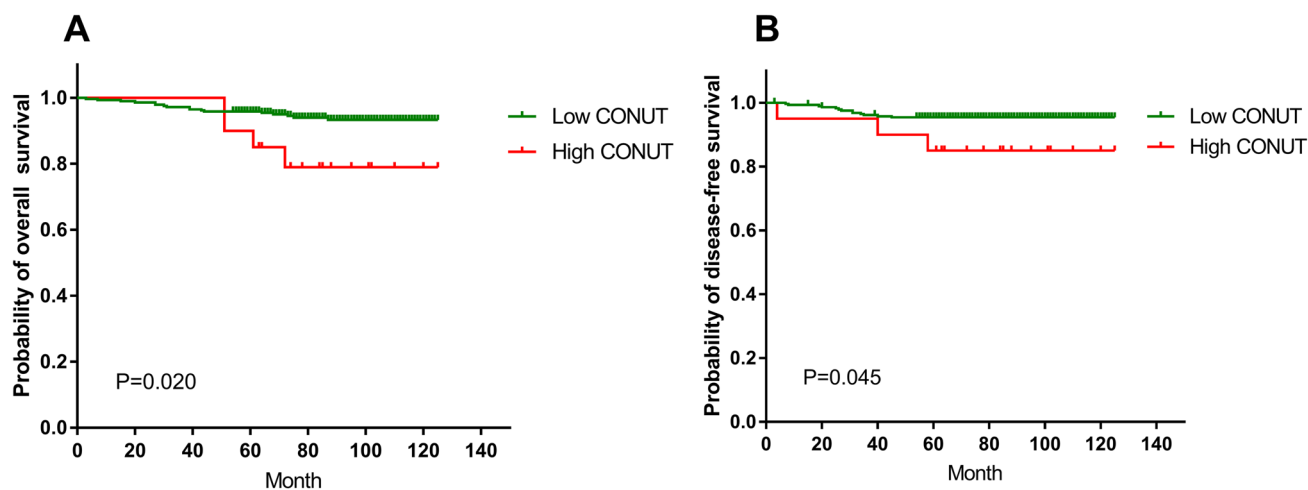
Fig. 2 Survival rates between high and low CONUT groups. **A** Overall survival in the two groups. **B** Disease-free survival in the two groups
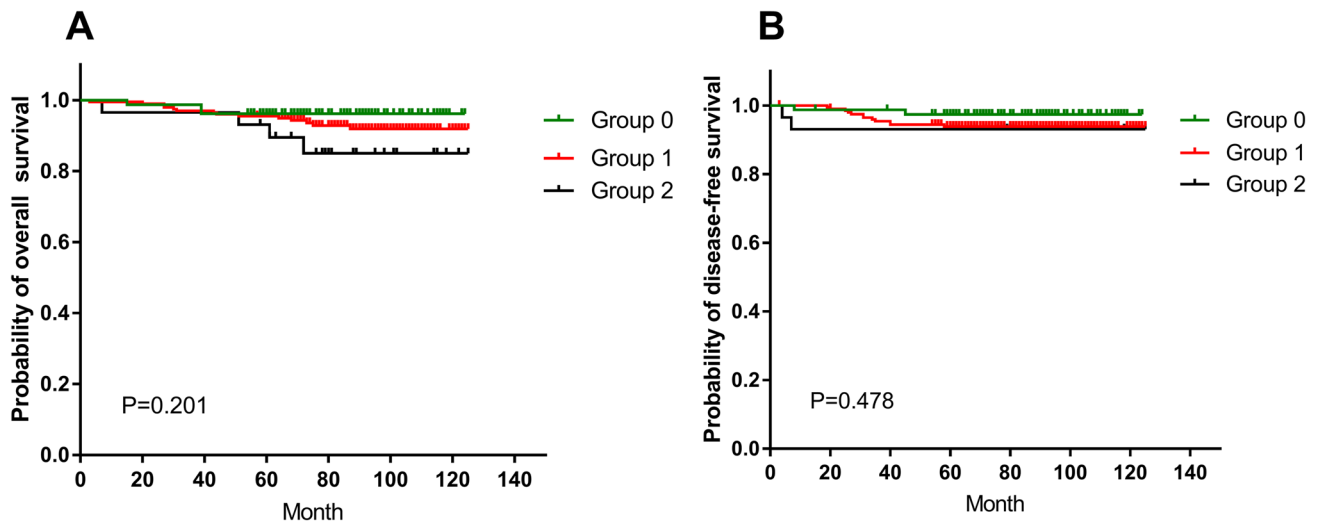
Fig. 3 Survival rates in the 0, 1, and 2 NPS groups. **A** Overall survival in the three groups. **B** Disease-free survival in the three groups

Relationships between PNI and clinicopathological characteristics

In the low PNI group, the proportions of patients with age > 63, CEA > 5.0 ng/ml, and albumin < 3.5 g/dl were significantly larger than in the high PNI group ($P = 0.001$, $P = 0.029$, and $P = 0.002$, respectively) (Table 5).

Discussion

Although stage I (T1-2N0M0) CRC generally has a good prognosis because it has superficial tumor invasion and absence of regional lymph node metastasis, a chance of recurrence remains after radical resection. Due to the low incidence of recurrence and death, regular postoperative

**Table 3** Univariate analysis for overall survival and disease-free survival

	Univariate analysis for overall survival			Univariate analysis for disease-free survival		
	Hazard ratio	95%CI	*P*-Value	Hazard ratio	95%CI	*P*-Value
Sex (male vs female)	1.118	0.471–2.654	0.800	0.666	0.231–1.917	0.451
Age (≤ 63 vs > 63)	4.846	1.630–14.405	0.005	1.862	0.677–5.124	0.229
BMI (< 25 vs ≥ 25 kg/m^2)	0.661	0.242–1.806	0.420	1.286	0.467–3.539	0.626
Histology (well/moderately vs poorly)	3.020	0.702–12.983	0.137	2.013	0.266–15.240	0.498
Location (colon vs rectum)	1.848	0.778–4.385	0.164	2.336	0.849–6.427	0.100
Tumor size (≤ 2 vs > 2 cm)	1.368	0.576–3.248	0.477	0.631	0.229–1.737	0.373
T stage (T1 vs T2)	1.580	0.666–3.750	0.299	1.537	0.572–4.126	0.394
Number of retrieved LNs (< 12 vs ≥ 12)	0.780	0.323–1.886	0.582	0.742	0.270–2.042	0.564
Lymphatic invasion (negative vs positive)	1.488	0.438–5.053	0.524	2.081	0.593–7.304	0.252
Perineural invasion (negative vs positive)	10.461	1.380–79.304	0.023	18.461	2.432–140.108	0.005
CEA (≤ 5.0 vs > 5.0 ng/ml)	1.774	0.522–6.023	0.358	2.659	0.758–9.330	0.127
Albumin (< 3.5 vs ≥ 3.5 g/dl)	0.188	0.025–1.406	0.104	0.141	0.019–1.069	0.058
PNI (≤ 49.3 vs > 49.3)	0.118	0.050–0.278	< 0.001	0.097	0.036–0.260	< 0.001
CONUT (< 3 vs ≥ 3)	3.373	1.135–10.026	0.029	3.353	0.955–11.766	0.059
NPS			0.224			0.501
0	1			1		
1	1.839	0.528–6.399	0.338	2.343	0.524–10.467	0.265
2	3.677	0.823–16.431	0.088	1.846	0.388–19.563	0.311

BMI body mass index, *LN* lymph node, *CEA* carcinoembryonic antigen, *PNI* prognostic nutritional index, *CONUT* controlling nutritional status score, *NPS* Naples prognostic score

**Table 4** Multivariate analysis for overall survival and disease-free survival

	Hazard ratio	95% CI	*P*-value
Model 1 — Overall survival			
Age (≤ 63 vs > 63)	4.265	1.405–12.948	0.010
Histology (Well/Moderately vs Poorly)	2.186	0.498–9.595	0.300
Location (Colon vs Rectum)	1.684	0.695–4.085	0.249
Perineural invasion (Negative vs Positive)	5.151	0.636–41.735	0.125
Albumin (< 3.5 vs ≥ 3.5 g/dl)	0.318	0.041–2.446	0.271
Model 2 — Overall survival			
Age (≤ 63 vs > 63)	2.853	0.917–8.876	0.070
Histology (Well/Moderately vs Poorly)	4.497	0.928–21.796	0.062
Location (Colon vs Rectum)	1.270	0.518–3.114	0.602
Perineural invasion (Negative vs Positive)	3.242	0.400–26.251	0.270
PNI (≤ 49.3 vs > 49.3)	0.141	0.054–0.371	< 0.001
Model 3 — Overall survival			
Age (≤ 63 vs > 63)	4.159	1.371–12.617	0.012
Histology (Well/Moderately vs Poorly)	2.359	0.531–10.478	0.259
Location (Colon vs Rectum)	1.722	0.712–4.166	0.228
Perineural invasion (Negative vs Positive)	3.371	0.391–29.047	0.269
CONUT (< 3 vs ≥ 3)	2.393	0.756–7.577	0.138
Model 4 — Disease-free survival			
Location (Colon vs Rectum)	2.151	0.750–6.171	0.154
Perineural invasion (Negative vs Positive)	13.785	1.707–111.328	0.014
CEA (≤ 5.0 vs > 5.0 ng/ml)	2.631	0.686–10.092	0.159
Albumin (< 3.5 vs ≥ 3.5 g/dl)	0.244	0.027–2.171	0.206
Model 5 — Disease-free survival			
Location (Colon vs Rectum)	1.737	0.603–5.004	0.306
Perineural invasion (Negative vs Positive)	20.084	2.126–189.717	0.009
CEA (≤ 5.0 vs > 5.0 ng/ml)	1.584	0.416–6.031	0.500
PNI (≤ 49.3 vs > 49.3)	0.105	0.037–0.297	< 0.001
Model 6 — Disease-free survival			
Location (Colon vs Rectum)	2.217	0.781–6.293	0.135
Perineural invasion (Negative vs Positive)	12.386	1.465–104.741	0.021
CEA (≤ 5.0 vs > 5.0 ng/ml)	2.783	0.765–10.125	0.120
CONUT (< 3 vs ≥ 3)	2.893	0.800–10.462	0.105

CEA carcinoembryonic antigen, *PNI* prognostic nutritional index, *CONUT* controlling nutritional status score
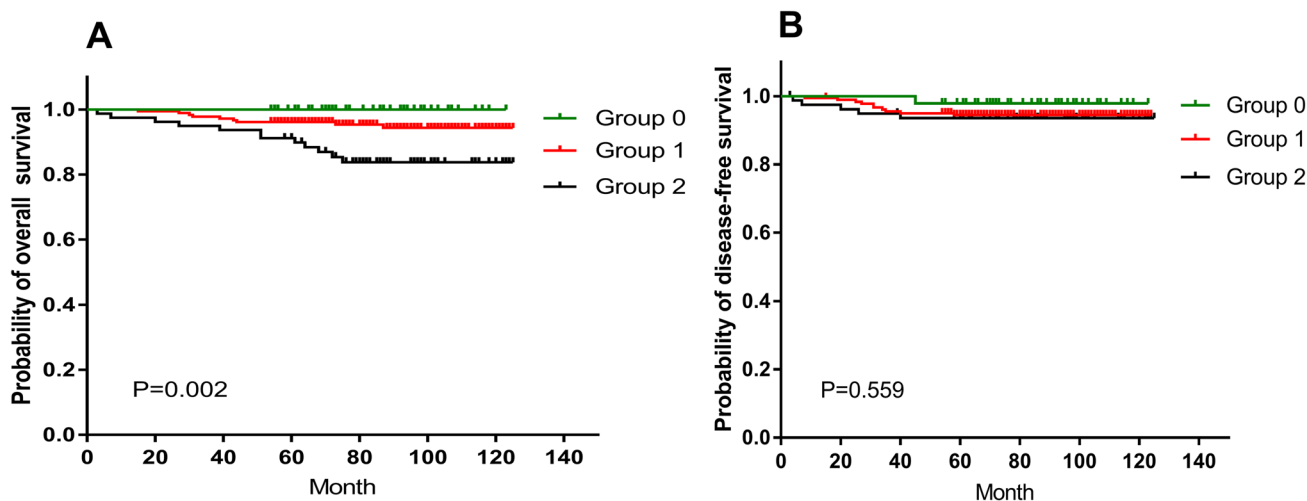
Fig. 4 Survival rates in the 0, 1, and 2 new-NPS groups. **A** Overall survival in the three groups. **B** Disease-free survival in the three groups
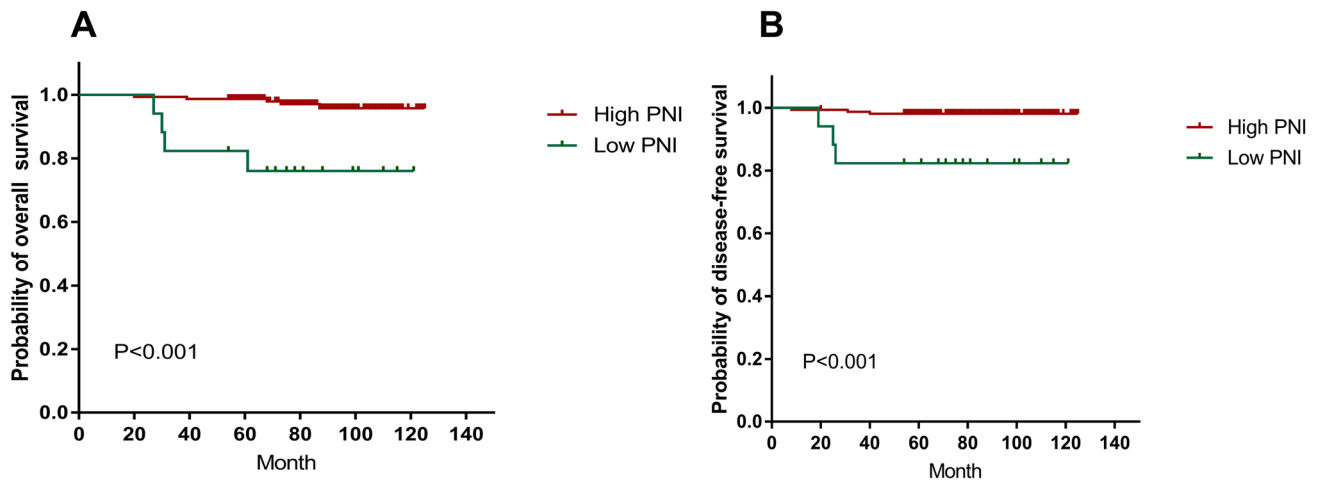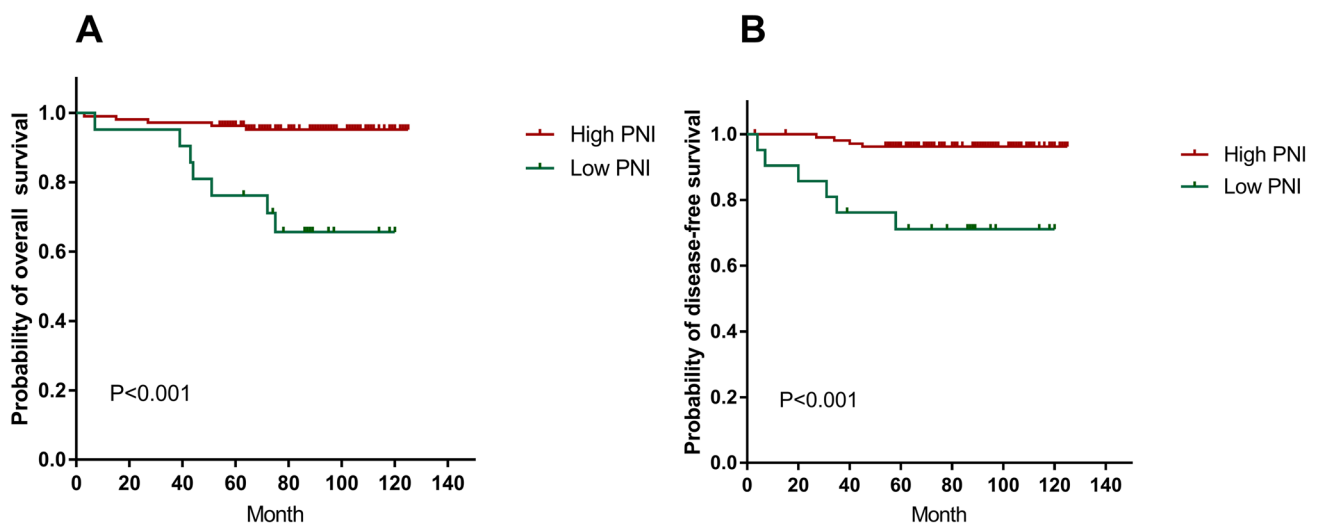
Fig. 5 Survival rates between high and low PNI groups in colon cancer. **A** Overall survival in the two groups. **B** Disease-free survival in the two groups

follow-up usually is not performed in clinical practice, resulting in lack of follow-up data for stage I disease [14]. Therefore, few studies consider stage I disease, and the risk factors have not been sufficiently evaluated.

Nutritional and immunologic statuses are closely associated with tumor growth, metastasis, and recurrence. Various nutritional and immunological status indicators that can be calculated from host serum markers have been established to predict prognosis [7–9]. If those easy-to-use serum indicators effectively predict outcome, clinical management of malignancies could be improved. The PNI, which is calculated using serum albumin and total lymphocyte count, has been reported as a predictor in various cancers including CRC [7, 15, 16]. The CONUT, which is

based in serum albumin, total lymphocyte count, and total cholesterol concentration, also has been reported to be independently associated with the survival rate of patients with various cancers including CRC [17–19]. Since 2017, the NPS based on serum albumin, total cholesterol concentration, NLR, and LMR has been reported as a predictor in CRC [9, 20]. Most previous studies evaluated those indicators in cohorts containing patients in stages I to IV. Disease progression at different stages produce different nutritional and immunological statuses, and treatment strategies at each stage are also different. Therefore those indicators should be evaluated at each stage. Although stage I CRC has a good prognosis, treatment strategies based on risk factors may further improve the survival.

Fig. 6 Survival rates between high and low PNI groups in rectal cancer. **A** Overall survival in the two groups. **B** Disease-free survival in the two groups

Table 5 Relationship between preoperative PNI and clinicopathological features

Variables	PNI ≤ 49.3 (N=38)	PNI > 49.3 (N=267)	P value
Sex			0.436
Male	25 (65.79)	158 (59.18)	
Female	13 (34.21)	109 (40.82)	
Age			0.001
≤ 63	10 (26.32)	148 (55.43)	
> 63	28 (73.68)	119 (44.57)	
BMI			0.988
< 25 kg/m^2	26 (68.42)	183 (68.54)	
≥ 25 kg/m^2	12 (31.58)	84 (31.46)	
Location			0.084
Colon	17 (44.74)	159 (59.55)	
Rectum	21 (55.26)	108 (40.45)	
Histology			0.371
Well/Moderately	38 (100)	256 (95.88)	
Poorly	0	11(4.12)	
Tumor size			0.398
≤ 2 cm	17 (44.74)	139 (52.06)	
> 2 cm	21 (55.26)	128 (47.94)	
T stage			0.586
T1	22 (57.89)	142 (53.18)	
T2	16 (42.11)	125 (46.82)	
Number of retrieved LNs			0.663
< 12	13 (34.21)	82 (30.71)	
≥ 12	25 (65.79)	185 (69.29)	
Lymphatic invasion			1.000
Negative	34 (89.47)	240 (89.89)	
Positive	4 (10.53)	27 (10.11)	
Perineural invasion			0.234
Negative	37 (97.37)	266 (99.63)	
Positive	1 (2.63)	1 (0.37)	
CEA			0.029
≤ 5.0 ng/mL	31 (81.58)	248 (92.88)	
> 5.0 ng/mL	7 (18.42)	19 (7.12)	
Albumin			0.002
< 3.5 g/dl	3 (7.89)	0	
≥ 3.5 g/dl	35 (92.11)	267 (100)	

BMI body mass index, *LN* lymph node, *CEA* carcinoembryonic antigen, *PNI* prognostic nutritional index

Serum albumin is produced by hepatocytes, and its production is inhibited by cancer-related pro-inflammatory cytokines such as interleukin-6, interleukin-1, and tumor necrosis factor-α, which eventually leads to cancer cachexia [21]. Serum albumin, which represents both nutrition status and disease severity, has been reported to be independently associated with survival rate of several cancers [22]. In the present study, all of the patients were not given nutritional supplementation before surgery, and only 3 (0.98%) patients with albumin < 3.5 g/dl. In the multivariate analysis, considered interactions between albumin and other scoring systems, we found that serum albumin was not independently associated with OS or DFS. Lymphocytes play a key role in cellular immunity. A low lymphocyte count can indicate poor immunologic function, and an insufficient immune response will promote tumor progression [23, 24]. In the present study, the PNI, which was calculated using albumin, total lymphocyte count, was independently associated with both OS and DFS; patients with low PNI had significantly worse OS and DFS than those with high PNI. Therefore, the prognostic value of PNI which represents nutritional and immunologic status was better than that of albumin in patients with stage I CRC. In addition, because our cohort included colon and rectal cancer, we conducted survival analysis according to the tumor location. We found the low PNI group had significantly worse OS and DFS both in the colon and rectal cancer.

In the present study, the cut-off values of PNI, CONUT, and NPS were in line with previous studies [7–9], but the results showed that PNI had a better prognostic value than CONUT and NPS in stage I CRC. In addition, unlike PNI and CONUT that had been reported as risk factors in various cancers, the NPS had been established and evaluated only in the two studies about CRC [9, 20]. Therefore, we re-determined the NPS and found it still was not associated with OS or DFS. Among the previous studies of CONUT, the study by Ahiko et al. [25] included the largest number of patients with stage I disease (n = 224) but also included 606 patients with stage II–IV disease. About NPS, the study by Galizia et al. [9] evaluated the 562 patients with CRC, which included 139 patients with stage I disease. Although those studies found that CONUT and NPS results were independently associated with OS and DFS, we suggest that the prognostic value of these indexes be assessed separately at each stage, because disease progression at different stages produces different nutritional and immunological statuses, which could affect the prognostic value of these indexes. Their cohorts contained only a small proportion of stage I patients, meaning that their cohorts had more severe disease than those in our study, in other words, their nutrition and immune conditions might be worse than in our cohort, which could improve the prognostic value of CONUT and NPS results. Although previous studies reported that the new CONUT and NPS indicators were predictors in CRC, the present study showed that these new indicators were not independent risk factors for stage I CRC, which is not robust and requires further research.

In summary, the PNI is a robust and effective risk factor in stage I CRC. In stage I CRC, the patients with low PNI might benefit from efforts to improve nutritional and immunological status before surgery, and a strong follow-up system should be followed during the postoperative period.

Some limitations of this study should be mentioned. First, this study was a retrospective single-center study with a small cohort, producing likely selection bias. Future multi-center, large-scale cohort studies or prospective, large-scale cohort studies are warranted to establish whether our results are robust. Second, in this study, C-reactive protein was not collected from most patients, so we did not include the modified Glasgow prognostic score which has been reported as a predictor in CRC [26, 27]. Despite those limitations, this is the first study to our knowledge to evaluate the prognostic significance of PNI, CONUT, and NPS results in patients with stage I CRC.

Conclusion

This study showed that the PNI is a simple and effective predictor of long-term survival in patients with stage I CRC, whereas CONUT and NPS are not. In stage I CRC, follow-up strategies and treatment plans based on PNI could bring great benefits to clinical practice.

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Data availability The dataset of the current study is available from the corresponding author on reasonable request.

Code availability Not applicable.

Declarations

Ethics approval This study had full ethical approval from the Institutional Review Board of Ajou University School of Medicine.

Conflict of interest The authors declare no competing interests.

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